

PSJ15 Exh 31

Specialty Pharmaceuticals Frequently Asked Questions – April 6, 2011

NOTE: We are providing the information in this FAQ for you to use either (1) in response to specific, unsolicited questions from a health care professional or (2) in specific objection handling related to these questions during a detail. Do NOT incorporate this information into your formal detail (i.e., do NOT use this information to make product claims) for either EXALGO or PENNSAID. Please contact your District Manager if you have questions.

EXALGO

Q: Can patients use the co-pay discount card more than once in the same month? For example: if a patient is being titrated and receives a prescription for 8mg for 2 weeks then is titrated to 12mg, can the patient use the discount card for both prescriptions?

A: Yes, the patient can use the co-pay discount card for all eligible prescriptions.

Q: Some physicians will challenge the dollar amount of the co-pay discount card, stating that other ER products have a better discount. Can marketing look at increasing the discount amount?

A: This question has a 2 part answer:

- When developing our discount program, marketing reviewed other competitor's discount card programs. What we found was that majority of programs had limited uses, required patients to register or required patients to pay a certain amount before the co-pay card discounted their prescription. Our co-pay card is SIMPLE; a flat \$25 discount, with unlimited uses, it can be used on every eligible EXALGO prescription.
- The idea of simplicity was echoed in our market research, physicians stated that they preferred a program that was easy to understand and easy to use.

Q: Are there any talking points for when a physician challenges dosing flexibility?

A: 1. Although the strengths are 8mg, 12mg, and 16mg, the dosing range studied in clinical trials is 8mg to 64mg.

2. Typically multiple tablets of the same strength to achieve a dose (eg. 2 - 16mg tablets to comprise a 32mg dose) would only constitute one co-pay for most payers, if dispensed at the same time.

Q: If a patient is prescribed 2 – 16mg tablets for a 32mg dose, should the patient take both 16mg tablets at the same time?

A: Yes. This product has been studied with once daily dosing. There is no data for twice daily dosing or other dosing regimes.

Q: What is the maximum daily dose of EXALGO?

A: The doses tested ranged from 8-64 mg, but there is no ceiling dose for hydromorphone. Hydromorphone is titrated up to effect and side-effects.

Q: Can you use breakthrough pain medications with EXALGO?

A: Yes, but consult the package insert before combining medications with your patient.

Q: What other proprietary products use OROS technology?

A: There are approximately 13 including Procardia XL, Glucotrol XL, Concerta, Invega, Ditropan XL, and Covera HS.

Q: What happens if EXALGO is crushed?

A: The tablet would be disrupted and the entire dose would be available which could lead to potentially serious or even fatal respiratory depression.

Q: Is there an EXALGO Patient Assistance Program?

A: Yes. The phone number for the Patient Assistance Program is 1-800-259-7765.

Q: Why are you recommending 50% of equipotent dosage and can it be safely initiated at a higher percentage?

A: This is what is approved by the FDA and it is consistent with many of other extended release opioids. Care should be taken to ensure adequate supplemental analgesics are also provided. Contact Medical Affairs for any further questions.

Q: Since the half life is 11 hours, can EXALGO be dosed BID?

A: While the half life may be 11 hours, the OROS technology in EXALGO releases the product over 2-16 hours. The product has not been studied for more than once daily dosing and it is not approved for BID dosing. Contact Medical Affairs for any further questions.

Q: Are there sulfites in the tablet formulation?

A: Yes. Contact Medical Affairs if you have additional questions or require further explanation.

Q: Does the sodium metabisulfite cause a contraindication in patients with sulfonamide allergies?

A: This may be a risk in patients with sulfonamide allergies. Contact Medical Affairs if you have additional questions or require further explanation.

Q: Is the risk of seizures with EXALGO greater than that of IR hydromorphone?

A: Contact Medical Affairs to provide information related to this question.

Q: How do the adverse events of EXALGO compare to other ER opioids?

A: The most common adverse events with EXALGO are the same type as seen with other opioids. EXALGO's nondeformable tablet makes it have some unique properties compared to other opioids, and as a result, additional warnings and precautions.

Q: Why are the MAO inhibitors contraindicated with EXALGO?

A: MAO inhibitors may exacerbate potentially severe adverse events, if taken with EXALGO or any opioid analgesic. Contact Medical Affairs for any further questions.

Q: What is the recommended dosing for gastric bypass patients?

A: EXALGO is contraindicated in these patients because of the nondeformable nature of the tablet.

Q: What safety concerns exist with EXALGO in patients with severe COPD/dyspnea?

A: Respiratory depression is the chief hazard of EXALGO. Use only with extreme caution in patients with conditions accompanied by decreased respiratory reserve. In these patients, even moderate therapeutic doses of hydromorphone may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnea. In these patients, consider alternative non-opioid analgesics, and use EXALGO only under careful medical supervision at the lowest effective dose. (See Section 5.3 in the PI)

Q: Can EXALGO be dialyzed?

A: Hydromorphone can be dialyzed although this has not been studied specifically in EXALGO. Contact Medical Affairs if you have additional questions or require further discussion.

Q: Does severe constipation affect the rate of release or absorption of EXALGO?

A: This has not been studied. Contact Medical Affairs for additional information.

Q: What is the amount of pressure required to crush EXALGO?

A: The tablet requires approximately 18 lbs of pressure to crush.

Q: Is EXALGO tamper resistant or abuse deterrent?

A: EXALGO, like all the other extended-release opioids on the market cannot claim to be tamper proof or resistant. In fact, the FDA has not clearly defined what constitutes tamper resistance in terms of clinical requirements. EXALGO can be tampered with for purposes of abuse. This is why it is so critical that proper patients be selected for EXALGO, like all the other extended-release products. Contact Medical Affairs if you have additional questions or require further discussion.

Q: Will there be future reformulations that include abuse deterrents?

A: We are constantly evaluating the product to optimize the life cycle of the brand.

Q: Is there a way for patients to tamper with EXALGO?

A: There are ways for individuals to destroy the extended-release technology to release the drug. Contact Medical Affairs if you have additional questions or require further discussion.

Q: Is there any abuse and diversion data for Journista?

A: Contact Medical Affairs for questions about abuse and diversion data for Journista.

Q: What opioid receptors does EXALGO work on?

A: EXALGO, or the hydromorphone, predominantly affects the MU opioid receptors.

Q: Will EXALGO show up on Ameritox screens?

A: Yes. Contact Medical Affairs if you have additional questions or require further discussion.

Q: Will EXALGO show up on drug screens?

A: Yes. Contact Medical Affairs if you have additional questions or require further discussion.

Q: How long until onset and maximum effect with initial dosing?

A: In a single dose study, mean Tmax varied by strength. It was reported to be 12 hours for the 8mg and 16 hours for the remainder of dosage strengths. The time to onset for the first dose was not specifically studied.

Q: What % of hydromorphone remains in the tablet at the time it is excreted?

A: It varies by strength. Contact Medical Affairs if you have additional questions or require further discussion.

Q: Why are you saying the half life of EXALGO is longer than the half life of IR hydromorphone?

A: The sustained action of the drug delivery system causes the drug to be delivered throughout an extended period of time; therefore, it is the hydromorphone in this particular delivery system which achieves the ~11 hour half life.

Q: Does the OROS technology provide a bolus effect of medication?

A: No. The osmotic release technology provides a controlled delivery of the drug. Refer to the Master Sales Aid, particularly the pharmacokinetic graph on p. 3)

Q: Where is EXALGO absorbed in the GI tract?

A: This has not been specifically studied. However, OROS technology releases from 2-16 hours.

Q: What is the EXALGO tablet made of since it does not dissolve in the GI tract?

A: EXALGO delivers hydromorphone via the OROS technology. OROS consists of an osmotically active bi-layer core contained within a non-absorbable shell designed to release the drug at a controlled rate. The tablet shell is eliminated from the body in the patient's stool.

Q: How long before drug is released from the tablet?

A: It begins to be released after 2 hours.

Q: Are there comparative studies of EXALGO vs. other ER opioids?

A: There are studies so please contact Medical Affairs for additional information.

Q: What breakthrough medications have been studied with EXALGO?

A: In our pivot trial, immediate release hydromorphone was used. Contact Medical Affairs if you have additional questions or required further discussion.

Q: Is there data studying dosing of EXALGO more frequently than Q24H?

A: No. The studies were all conducted with once daily dosing and as such the FDA approved EXALGO for once daily dosing.

Q: Why did EXALGO and placebo have drug withdrawal adverse events in 301?

A: This has not been determined. However, one possible reason is the placebo group still received breakthrough meds.

Q: Is there clinical data supporting the 24 hour dosing of EXALGO?

A: Yes. Reps will soon be receiving the 301 trial reprint and carrier, which provides clinical support for the once daily dosing.

Q: What is the rate at which Exalgo is released?

A: Hydromorphone is released in a constant rate of 5% to 7% per hour from hours 2 through 18. Hydromorphone release is independent of pH and GI motility.

Turgeon J, Groning R, Sathyan G, Thippawong J, Richarz U. The pharmacokinetics of a long-acting OROS hydromorphone formulation. *Expert Opin Drug Deliv.* 2010;7:137-144.

Keep in mind it does not speak to metabolism of hydromorphone

Q: What is the average co-pay for EXALGO?

A: According to our available claims data, about 80% of EXALGO patients pay a net co-pay of \$50 or less.

Q: How can you convert a patient from IV hydromorphone to EXALGO?
A: There are no available studies suggesting how to convert patients from IV hydromorphone to EXALGO. We suggest to consider converting the patient first from IV hydromorphone to immediate release hydromorphone and then once stabilized convert them at a 1:1 ratio of immediate release hydromorphone to EXALGO.

PENNSAID

Q: What is DMSO?

A: DMSO stands for Dimethyl Sulfoxide. A long recognized chemical compound that has been used in pharmaceuticals as well as other areas of manufacture.

Q: What is Procipient®?

A: Procipient® is a highly purified version of DMSO that is commercially available. -It is the DMSO used in PENNSAID®

Q: What does "highly purified" mean?

A: It is produced under current Good Manufacturing Practice (cGMP) protocols to conform to USP and PhEur standards. It is pharmaceutical grade! These protocols and standards are recognized by the FDA.

Q: Is this different than the DMSO used on animals?

A: There are products that are FDA approved for veterinary use that contain DMSO. However, many people are familiar with DMSO that can be purchased at trade shows or farm stores. This DMSO is NOT the purified version found in PENNSAID and not the FDA approved veterinary medications.

Q: Is DMSO an abused medication?

A: No. DMSO is not a controlled substance nor is it an abused medication. However, it has been used in compounding pain and anxiety medications for hospice patients and used as a method for delivery for illicit substances by people who abuse drugs. The 45.5% DMSO contained within PENNSAID would generally not be considered as desirable by those using illicit substances. In addition PENNSAID is only available in a 5 oz bottle and is significantly more expensive than larger quantities available as direct to consumer products.

Q: Is DMSO prohibited in athletes?

A: DMSO is not listed on the International Olympic Committee list of banned substances. This list is one of the most restrictive used in competitive sports.

Covidien has confirmed with the United States Anti-Doping Agency (USADA), the World Anti-Doping Agency (WADA), and the National Collegiate Athletic Association (NCAA) that DMSO is **NOT** a banned substance. The NCAA stated that since DMSO is not a banned substance and is not restricted to targeted therapy, there are no restrictions on its use in athletic organizations.

In addition, NSF International, the not-for-profit health and safety company that has a Certified for Sport program, does not test for DMSO since it does not have a banned/restricted status.

Q: Will PENNSAID pull toxins through my skin as I apply it?

A: Hands should be washed before and after the application of PENNSAID. The area PENNSAID is applied to should be clean and dry. Although DMSO is a known penetration enhancer, the molecule of a substance still must lend itself to penetrate the skin. Lipophilicity/hydrophilicity as well as the size of the molecule all contribute to the ease of penetration of the skin. Applying DMSO to one section of skin is not known to suddenly stimulate permeability to the entire surface of the body. Higher concentrations of DMSO are associated with increased transdermal penetration.

Q: Is DMSO carcinogenic?

A: DMSO is not a known or suspected carcinogen. It is not known to be a reproductive toxin nor mutagenic. In fact, DMSO is used as one of the solvents in the AMES test (a test for mutagenicity).

Q: What about Covidien's carcinogenicity trial?

A: The FDA has required Covidien to conduct an ongoing carcinogenicity trial for PENNSAID, the conclusion and results should be known in approximately 2 years. It is not unusual for the FDA to require post marketing or phase IV studies after a product is launched.

Q: Is DMSO an API or an excipient?

A: DMSO can be either an API or an excipient. In PENNSAID it is a vehicle or excipient. The pivotal studies showed it to have no therapeutic effect.

Q: Do we need to instruct patients to wash their hands prior to PENNSAID application since the DMSO has the ability to bring molecules, possible unwanted substances, into the body?

A: As indicated by the PI, patients should always be instructed to wash their hands prior to application, and apply PENNSAID to clean, dry skin.

Q: Although PENNSAID has no known effect on platelet aggregation, should PENNSAID be used with caution or not at all in patients currently taking Coumadin or Plavix?

A: The physician should be referred to medical affairs to address this question.

Q: What is the onset of action for PENNSAID?

A: According to the PI, following a single dose of PENNSAID (80 drops, two knees), the T_{max} (time to maximum plasma concentration) is 11.0 ± 6.4 hours. Following a multiple dose of PENNSAID (80 drops, QID, 7 days), the T_{max} is 4.0 ± 6.5 hours.

[If pressed by the HCP: Typically, transdermal delivery systems accumulate a reservoir of drug in the skin. Multiple applications of a topical can be expected to shorten the T_{max}. Data suggests this is occurring with PENNSAID as well. Data suggest that on-set of action will greatly vary by patient].

Q: How long does it take PENNSAID to reach steady state levels in the blood stream?

A: According to a published report, following application of 80 drops, two knees, QID, for 7 days, steady state was reached on day 6.

Q: What is the half-life of PENNSAID?

A: According to the PI, mean half life was 37 hours following a single dose of 80 drops (40 drops per knee), and was 79 hours following multiple applications of 80 drops for 7 days.

Q. How many days before surgery should a patient stop using PENNSAID?

A. As stated in the PI, there was no effect on platelet aggregation after application of the maximum clinical dose for 7 days (80 drops, two knees, QID). Any questions beyond this should be referred to Medical Affairs.

Q. Why does PENNSAID contain 1.5% Diclofenac?

A. During its development, the innovators of PENNSAID conducted clinical trials utilizing various concentrations of diclofenac. Based on the collective clinical trial data, 1.5% w/w diclofenac was determined to be the most effective.

Q. What does gtts mean?

A. A drop is abbreviated *gtt*, with *gtts* used for the plural. These abbreviations come from *gutta*, the Latin for drop.

Q. Please clarify the difference in dry skin adverse events from what is seen in the PI (32%) and Simon (18%).

A. Data contained within the PI reflect the complete exposure data available for a product at time of approval. The 32% represents exposure to PENNSAID in 911 patients treated between 4 and 12 weeks in seven Phase 3 clinical trials (published and non-published), as well as exposure of 793 patients treated in an open label, long-term study. The data from the Simon study is one clinical trial of 12 weeks, in 154 subjects (PENNSAID arm only).

Q. Please clarify the dry time for PENNSAID.

A. Drying time is known to vary by patient and patients should wait until the knee is completely dry to apply other topical lotions. It has been reported that the treated knee is typically dry after 10 minutes. Patients should wait at least 30 minutes before showering or bathing after applying PENNSAID.

Q. Why is the placebo effect so high in both the Simon and Roth studies?

A. In any clinical studies, it is understood that some patients will experience a 'placebo effect'. In addition, in both studies acetaminophen was provided and permitted which may have contributed to the placebo effect, although this has not been proven.

Q. How should I respond if a physician states he is going to use PENNSAID PRN (as needed)?

A. How PENNSAID should be dosed is a decision best made between the physician and the patient. If a physician indicates that he/she is only going to dose PENNSAID PRN, remind the physician it is indicated to be dosed 40 drops at a time, QID. That is as far as you need to take it.

Q. Will there be an application video contained on the website?

A. We are in the process of developing a patient application video which will be contained on the PENNSAID website –www.TreatKneeOA.com.

Q. What is the expiration of a bottle of PENNSAID 150 mL last once opened?

A. The FDA did not require open/close data once a bottle has been opened. Please refer to the stamped expiration date on the bottle. If used as indicated, one 150 mL bottle should provide a patient enough product to treat one OA knee for 30 days.

Q. Does PENNSAID stain clothing?

A. We are not aware of any reports of Pennsaid staining clothes.

Q. Can co-pay cards be used with other Medicare/ Medicaid patients?

A. No Co-pay cards, regardless of the manufacturer, can be used with any other US government funded program. It is illegal to knowingly adjudicate a patient co-pay card for any patient who participates in Medicare, MediCaid, Tri-Care (military) or any other federal healthcare program.

Q. Can co-pay cards be redeemed for cash?

A. No. Co-pay cards have no cash value, and can not be redeemed for cash.

Q. If more than one bottle of PENNSAID is prescribed per prescription, is the co-pay amount applied to each bottle?

A. The co-pay card program is adjudicated at the script level. Regardless of how many bottles are prescribed, the \$30 co-pay amount is applied to an individual prescription, once a month, for a total of 12 months

Q. How was Voltaren Gel measured to get 6% systemic levels?

A. We don't know for sure how these data were derived. However, it is our understanding that Novartis, the manufacturers of Voltaren Gel, derived these data from their PK study, but these results have not been published.

Q: Do we have any additional information on DMSO being removed from the market?

A: Investigational New Drug (IND) status was granted for DMSO in 1963 but the FDA banned studies in human subjects in 1965 due to safety concerns. However, in 1980 the FDA revoked their policy restricting DMSO research after the National Academy of Sciences (NAS) published findings in favor of DMSO in 1972. Please note, these safety concerns arose from a case report in Ireland in which no causal relationship was established.

Q: Does PENNSAID penetrate all the way into the synovial joint of the knee?

A: Since specific studies were not conducted measuring the presence or amount of diclofenac in the synovial joint, we can not say for certain whether DMSO or diclofenac penetrates all the way into the knee joint. However, we do know that application of PENNSAID results in a systemic absorption of diclofenac of ~3.3%, that there is a measurable Tmax, Cmax and AUC, and that the synovial membrane, which surrounds the joint and secretes synovial fluid, has a blood supply.

The FDA approved PENNSAID for the signs and symptoms of OA of the knee(s) since our clinical studies were able to demonstrate a consistent statistical difference in the reduction of pain, improvement in physical function and improvement in patient overall health assessment, all of which support the efficacy of the product.

Q: Who is Dr. Lee Simon, and why is he important (See Simon clinical reprint)?

A: Dr. Lee Simon, is a rheumatologist by training, and was a longstanding professor of Rheumatology at Harvard University. Dr. Simon was formally a Division Director in the Center for Drug Evaluation and Research of the FDA. Following his work at the FDA, Dr. Simon joined the trial team of the 5 arm PENNSAID clinical study, and is the lead author of the pivotal paper. Dr. Simon has since left Harvard and now consults, but he is widely published and is still a leading member of the Osteoarthritis Research Society (OARSI) and the Outcome Measures in Arthritis Clinical Trials (OMERACT).

Q: How much diclofenac is absorbed into the skin?

A: The level of penetration of diclofenac into the skin has not been measured, and therefore is unknown. It is known that the systemic absorption of diclofenac in PENNSAID is approximately 3.3%.

Q: What studies exist demonstrating DMSO as a penetration enhancer?

A: Based on the current body of knowledge, DMSO is generally accepted as a known penetration enhancer. For example, Kolb and colleagues (1967) published a study that evaluated the absorption and distribution of radiolabeled DMSO in lower animals and man. In man, radioactivity appeared in the blood 5 minutes after cutaneous application. One hour after application of DMSO to the skin, radioactivity could be detected in the bones.

Q: What is the concentration of dose for 10 drops, i.e. how much diclofenac (mg) and DMSO (g)?

A: Each dose of PENNSAID (40 drops, 1.25 mL) contains approximately 20 milligrams of diclofenac and approximately .57 grams of DMSO. Therefore, 10 drops contains approximately 5 milligrams of diclofenac and approximately .14 grams of DMSO.

Q: Were the OA of the knee patients in the pivotal trials (Simon and Roth) considered to have mild, moderate or severe OA?

A: While neither Simon or Roth define patient's as having mild, moderate or severe OA of the knee, in the Simon study, patient selection was based upon:

- Standard radiological criteria for OA on a recent examination (within 3 months)
- Pain, with regular use of an NSAID (at least 3 days a week)
- Flare of pain (defined as an increase in total Likert pain score of 25%, and at least 2, and a score of at least moderate on one or more of the 5 question WOMAC pain scale)
- A minimum Likert pain score of 8 (40 on a scale normalized to 0-100) at baseline following washout of pain medication

In the Roth study, patient selection was determined by:

- Radiological findings of deterioration and abrasion of the articular cartilage and/or formation of osteophytes at the joint surface of the knee
- Flare of pain, defined as an increase on the pain subscale of at least 2 points and 25%, a score of at least 2 (moderate) on at least 1 of the 5 questions on the WOMAC pain scale, after washout of stable therapy at least 3 days per week for one month consisting of an oral NSAID or acetaminophen

Q: Should the sales reps record which physicians are provided a PENNSAID OA Knee Model?

A: Under PhRMA guidelines, a log must be kept of physicians who receive the knee model since it will have an assigned value. The knee model has been added to the drop down menu of the marketing items in Mobile Intelligence and should be recorded there.

Q. The PENNSAID PI states a 3.3% absorption rate. Since PENNSAID contains 1.5% Diclofenac, and Voltaren Gel contains 1.0%, shouldn't our absorption rate be higher than Voltaren Gel that has a 6% absorption rate?

A. Absorption rates can vary depending upon how the molecule distributes within the various skin layers. Clinical studies measuring the systemic level of PENNSAID have not been conducted. It is understood that transdermal delivery systems accumulate a reservoir of drug in the skin. Contact Medical Affairs for any further questions.

Q. Can PENNSAID be used with Coumadin (warfarin)?

A. Drug interactions with the use of PENNSAID have not been studied. Refer the health care provider to section 7.2 of the PENNSAID PI, drug interactions with anticoagulants such as warfarin. Contact Medical Affairs for any further questions.

Q. Does patient weight or size affect absorption levels? If so, does dosing need to be adjusted?

A. The PENNSAID clinical studies make no reference to patient size and/or weight. At this time it is unknown if obesity impacts PENNSAID absorption. Regardless, physicians should continue to educate patients on the approved dosing of 40 drops per knee(s), QID.

Q. Does 'fluid' in the knee affect absorption levels?

A. It is not known if patients with 'fluid on the knee' were included in the clinical trials, and so it is unknown if absorption rates would be affected. As with obese/ physically large patients, physicians should still follow the approved dosing of 40 drops per knee(s), QID.

Q. Is PENNSAID as effective applying 40 drops just to the front of the knee instead of having to apply to all four sides of the knee?

A. Patients should be instructed to apply PENNSAID to all four sides of the knee(s), since this is the manner in which the clinical studies were conducted and efficacy results measured. Since OA of the knee affects the entire knee, applying PENNSAID to just the top of the knee could impact the effectiveness of the product.

Q. How long should patients avoid natural or artificial sunlight after applying PENNSAID?

A. The PENNSAID PI instructs patients to avoid exposure to natural or artificial sunlight while using PENNSAID. However, sunscreen can be applied to the knee once PENNSAID is completely dry thus minimizing or avoiding exposure.

Q. What is the percentage of patients who have OA of the knee in both knees?

A. In patients with OA of the knee, it is estimated that the prevalence of generalized osteoarthritis of both knees is 87%. In the Simon study, the incidence of bilateral OA of the knee was over 95%.

Q. Can PENNSAID be used in patients with knee replacement?

A. PENNSAID is indicated for the signs and symptoms of OA of the knee(s). Clinical studies have not been conducted in patients who have had a knee replacement.

Q. Can PENNSAID cause numbness in hands when applying?

A. According to the PI, 2% of patients experienced non-application site (other than the knees) paresthesia (numbness). When detailing your physicians, remember to inform them that patients should always wash their hands with soap and water before and after applying PENNSAID.

Q. What is the maximum daily dose for PENNSAID?

A. The maximum daily dose of PENNSAID is 40 drops per affected knee, four times a day. If treating bilateral OA of the knee, this would be 40 drops, four times a day on each knee.

Q. What is the recommended dose of PENNSAID when applied to other joints?

A. PENNSAID is only indicated for the signs of symptoms of OA of the knee(s). Clinical studies have not been conducted on any joint other than the knee. If health care providers have questions beyond our indication, please refer them to Medical Affairs.

Q. What oral pain relief products can be used in conjunction with PENNSAID?

A. Patients should avoid concurrent use of PENNSAID with oral NSAIDs. In both of the pivotal trials (Simon and Roth), concomitant analgesic and anti-inflammatory medications, including over-the-counter NSAIDs and other analgesics, were prohibited. However, rescue analgesia with acetaminophen, up to four 325-mg tablets per day, was permitted. Any other questions regarding the concomitant use of oral pain relief products should be referred to Medical Affairs.

Q. Is PENNSAID safe to use in conjunction with therapeutic ultrasound?

A. This has not been studied and should be referred to Medical Affairs.

Q. How long must a patient wait after applying PENNSAID before applying a heat compress?

A. According to the PI, do not apply external heat and/or occlusive dressings to the treated knee(s). Heat is often used to loosen stiffened joints. However, combined with a topical agent, it could burn the skin or alter its rate of transdermal absorption or delivery.

Q. Is PENNSAID safe to use with intra-articular injections?

A. This has not been studied, and should be referred to Medical Affairs.

Q. Is PENNSAID safe in liver-transplant patients?

A. This has not been studied, and should be referred to Medical Affairs.

Q. Is PENNSAID safe in severely asthmatic patients?

A. Refer to section 5.10, Preexisting Asthma, in the PENNSAID PI. Refer all other questions to Medical Affairs.

Q. What is the pharmacokinetics of doses >320 drops per day (80 doses QID)?

A. The maximum daily dose studied was 320 drops per day (i.e. 160 drops per knee per day). Amounts exceeding 320 drops, either to the treated knee(s) or to other joints, have not been studied.

Q. Have there been any long term safety studies conducted with PENNSAID?

A. Yes. In an open label study, 463 patients were treated for at least 6 months and 144 patients treated for at least 12 months.

Q. Have any studies been conducted comparing PENNSAID to Voltaren Gel, or do we plan to conduct such studies?

A. Decisions regarding comparative studies have not been determined.

Q. Does the fact that Voltaren Gel has a higher systemic exposure rate (6% vs 3.3%) imply that the product could be more efficacious than PENNSAID?

A. Systemic exposure is a measure (or estimate) of the NSAID molecule (Diclofenac) in the bloodstream and not necessarily a measure of efficacy. Since studies have not been conducted comparing the efficacy of Voltaren Gel to PENNSAID, one can not make a claim that one product is more efficacious than the other. If this question comes up, redirect the physicians to what we do know about PENNSAID, focusing on the efficacy data from Roth and Simon that PENNSAID is the only FDA approved topical NSAID which demonstrated statistically significant differences in the outcome measures of all 3 primary efficacy variables: pain, physical function and POHA and PGA.

Q. Will the PENNSAID PI need to be revised due to the FDA's new warnings and precautions about the potential for elevation in liver function tests during treatment with all products containing diclofenac sodium?

A. No changes have been proposed by the FDA.

Q. Does DMSO act as a pain reducer if used by itself?

A. Based on the current body of knowledge, DMSO is generally accepted as a known penetration enhancer. In two pivotal studies, Simon and Roth, DMSO at 45.5% w/w showed no therapeutic effect on its own.

Q. Since PENNSAID® is only indicated for one joint (knee), why would a physician consider PENNSAID when Voltaren Gel® is indicated for more than one joint?

A. Please respond with the following, "Doctor, you may be prescribing topical NSAIDs over oral forms because you have concerns about your patient's systemic exposure to diclofenac. For patients presenting OA in multiple joints, please be mindful that your patients do not exceed the maximum recommended total body dose of product, regardless of what topical you prescribe. For example, a patient who has applied either Voltaren Gel or PENNSAID to both knees at the same time in accordance with the full Prescribing Information has already received the maximum total body dose of topical NSAID as recommended in their respective package inserts. Note also that systemic exposure for PENNSAID has been estimated to be about 3.3% as determined by comparison to the systemic exposure of Solaraze." (see section 12.3 of the PENNSAID PI which stated that, based on a one week study, PENNSAID is estimated to have 1/3 of the Solaraze systemic absorption, estimated to be 10%).

Q. What can you tell me about a recent study which states that patients who take Diclofenac are at a higher risk?

A. Please reinforce these three points when asked: a. All NSAID have risk and carry the same class wide Black box warning.

b. The study in question was a European retrospective study which only compared oral NSAIDs. No topical NSAIDs were included in the study.

c. Use of topicals has been recommended by a number of organizations, including European organizations, because of the presumed reduced systemic exposure compared to orals. PENNSAID is estimated to have a systemic exposure of approximately 3.3%

Q. How did you derive that PENNSAID has a 3.3% systemic absorption rate?

A. 3.3% is a calculated value, based on specific FDA findings from safety studies with Solaraze, a topical product containing much higher levels of diclofenac and is indicated for the treatment of actinic keratoses. With the established systemic exposure of Solaraze (10%), the FDA allowed data from a pharmacokinetic study with PENNSAID patients, prior to any therapeutic applications of Solaraze. Data showed that these patients experienced no PENNSAID related rates of increased diclofenac absorption. The FDA allowed the calculated systemic absorption rate of 3.3% (1/3) based on the safety findings with Solaraze.

Q: A Physician told me the standard apothecary measurement for 20 drops equals 1 cc (cc is an equal measurement to mL). How was it determined with PENNSAID that 40 drops equals 1.25mL?

A: Your physician is correct. 20 drops per 1 mL is the standard apothecary (historical name for a medical professional who formulates and dispenses medication to physicians, surgeons and patients — a role now served by a pharmacist) unit of measurement. However, the 20 drops is a function of the dropper size and the container from which it is dispensed. The PENNSAID bottle top utilizes a smaller drop dispenser. As a result, 40 drops from the tip of the PENNSAID dispenser equals ~ 1.25mL.

Q: Does obesity or body size effect the way PENNSAID works?

A: Doctor, although this specific population was not sorted as a group, all 5 core PENNSAID clinical studies had good representation of patient's with a body mass index (BMI) >30.

Q. Pharmacist are claiming it takes 60-90 days to receive their money when adjudicating patient co-pay cards from the 3rd party vendor. They claim they are losing money on every script. Is this true for the PENNSAID patient co-pay card?

A. Rx Sample Solutions is the vendor which manages the pharmacy reimbursement for the PENNSAID co-pay cards, and they reimburse pharmacies twice a month. In addition, the pharmacy makes \$2.25 on each co-pay card adjudication, so there should be no concern from pharmacist that they lose money on every script with a PENNSAID patient co-pay card.

Please note, all mail order pharmacies are set up to accept vouchers. Unfortunately the number of rebates processed is low due to the volume of scripts they fill every day. Rx Sample Solutions suggests we recommend patients purchase their medication via mail order, and then follow the instructions for mail in claims to RESTAT on the back of the voucher/card. RESTAT will then mail the patient a check in the amount of the rebate.

Q. How do I explain what weight/weight means?

A. As you recall, PENNSAID is expressed as diclofenac sodium topical solution 1.5% w/w. Weight to weight is a way of expressing concentration, namely, grams of solute (diclofenac) to grams of solution. Traditionally, most water based products are measured in weight to volume, but because PENNSAID contains a significant amount of nonaqueous liquids (DMSO and alcohol), weight to weight is a more precise measurement.

Q: Is PENNSAID contraindicated in other joints?

A: Use of PENNSAID in other joints would be off label use, not a contraindication for use of this product. Clinical studies of PENNSAID were only conducted on osteoarthritis (OA) of the knee, the most common form of OA.

Q: Is PENNSAID contraindicated in patients who have had a coronary artery bypass graft (CABG) surgery?

A: PENNSAID is only contraindicated in the perioperative period surrounding CABG surgery. Perioperative is defined as the period before the surgery or up to 14 days post surgery. Outside of this period, PENNSAID should be used with caution as the patient would fall into the cardiovascular risk category. The word "perioperative" is not consistently used throughout the PI. However, it is clear that PENNSAID is contraindicated during the perioperative period, and to be used with caution outside of this period for CABG surgery patients.

Q: Can PENNSAID be used while undergoing Iontophoresis (I-ahn-toe-for-E-sis) or Phonophoresis (Foe-no-for-E-sis)?

A: The use of Iontophoresis, using electricity to deliver medication through the skin and Phonophoresis, using ultrasound to enhance the delivery of topical medications, have not been studied with PENNSAID. However, any mechanism to enhance the delivery of a topical agent would alter its rate of transdermal absorption or delivery and, potentially, its efficacy and safety profiles. For further information, please contact Medical Information.

Q: Can the sales force have a bottle of PENNSAID for demonstration purposes?

A: The sales force now has access to empty 150mL trade bottles for demonstration purposes only. The bottles should only be used in conjunction with a PENNSAID detail in the physician's office, and should never be filled with any liquid.

Master Sales Aid

Q. How much PENNSAID was applied during the Franz Chamber study?

A. The recommended dosing for PENNSAID is 40 drops per application, QID, and each 40 drops of PENNSAID equates to approximately 1.25mL. In this particular study, 2.5 MICROLiters was applied to a 1 centimeter by 1 centimeter piece of human cadaver skin (1 MICROLiter = 1 thousandth of a milliliter (mL)). Though small, both the sample size and amount of PENNSAID applied is representative of the treated knee area and 40 drops. As a reminder, the study was designed to assess penetration, and not efficacy.

Q. What is the 12 month study and is it available for distribution?

A. The 12 month open-label study referenced on the Safety and Tolerability page of the Master Sales Aid assessed the safety and tolerability of PENNSAID when it was continuously dosed over a 6 and 12 month period (40 drops, QID). Results were published in The American Journal of Therapeutics in 2010 (Shainhouse et al). Currently there are no plans to make this particular study available as an approved leave behind.

Q. Do we have a study that shows PENNSAID vs. cardiac safety or for congestive heart failure (CHF) patients?

A. We do not have any studies comparing PENNSAID in cardiovascular patients, and any such questions should be directed to Medical Affairs.

Q. How was the 1/125th systemic exposure of PENNSAID to oral NSAIDs determined?

A. Data establishing the systemic exposure of PENNSAID to be 1/125th of oral diclofenac was first published in Bookman et al (Effect of a topical Diclofenac solution for relieving symptoms of primary OA of the knee: A randomized controlled trial). Bookman reports on results of two different clinical trials. In the first, a single application of PENNSAID was measured to be 12ng/mL, and in a second study, a comparable single dose of oral diclofenac was shown to have a systemic exposure of 1500ng/mL. Mathematically reducing the fraction of $12/1500 = 1/125$.

Q. Please explain in further detail the 3.3% systemic absorption of PENNSAID

A. In clinical trials, Solaraze, a 3% diclofenac sodium gel, indicated for the treatment of actinic keratosis, was shown to have a systemic exposure of 10%. It is understood that following the wash out period, patients from at least one of the Solaraze clinical trials then applied PENNSAID. With an established baseline of 10% systemic exposure with Solaraze, it was determined that the PENNSAID systemic exposure was 1/3 of the Solaraze exposure, or 3.3%. The FDA allowed the PENNSAID package insert to state that PENNSAID systemic exposure was approximately 1/3 of the diclofenac systemic exposure from Solaraze.

Q. How do you effectively utilize the C_{max}, T_{max}, AUC table data? Is key point the 1/125 of oral NSAIDS?

A. The data contained on the Safety and Tolerability page of the master sales aid established that PENNSAID has a relatively low C_{max} and AUC. As you recall from training, a relatively low C_{max} and AUC suggest low systemic absorption and potentially fewer adverse events. As a standalone set of data, this is meaningful to physicians.

Q. Why don't we have data comparing PENNSAID C_{max}, T_{max}, AUC to Voltaren Gel or oral diclofenac?

A. Since direct head to head comparison data between PENNSAID and Voltaren Gel do not exist, we cannot make any direct comparative claims. At this time we have decided to not display data end points comparing PENNSAID with oral diclofenac.

Q. Are there plans to distribute the Tugwell paper to the sales force at this time?

A. No. The Tugwell paper is a 2 arm efficacy study comparing PENNSAID to oral diclofenac. Our current position with the Tugwell paper is that we will not reference it to make comparative claims between PENNSAID and oral diclofenac, other than letting the physician know that the study exists. Please see page 5 of the master sales aid for an approved presentation of the relevant data in the Tugwell paper.

DMSO

Q. If someone has a Sulfur allergy, is there an issue with using DMSO?

A: The FDA approved package insert does not list sulfonamides (aka sulfa drugs) as an allergy or contraindication. However, one of DMSO's metabolites is a sulfone, which may produce allergic reactions in sulfonamide allergic patients, but not necessarily. Post marketing U.S. surveillance has identified one case of possible sulfa-type allergic reaction to date.

Q. How is DMSO dosed for interstitial cystitis (IC)?

A: Questions regarding the dosing of DMSO for interstitial cystitis should be directed to the appropriate manufacturer.

Q. Was the data from the new DMSO leave behind which depicts the creation of aqueous pores used in the development of the formulation of PENNSAID?

A. The two articles cited in the new DMSO leave behind that theorize DMSO's mechanism of action (see Notman et al and Gurtovenko et al) were both published well after PENNSAID was developed, so it is unlikely either had anything to do with how PENNSAID was developed.

Q. When applying PENNSAID, isn't it likely it might also penetrate thru the skin on the hand?

A. It is possible that some small amount of diclofenac could be absorbed during the application process if a bare hand is used, but this has not been studied. As directed in the patient med guide, patients should always wash their hands with soap and water before and after application of PENNSAID.

Q. In the Franz chamber penetration chart, why is the aqueous solution higher in the first 4 hours than PENNSAID?

A. When discussing the Franz chamber penetration chart, it is important to help physicians stay focused on the big picture. Following a single dose, the penetration difference between PENNSAID and aqueous solution diclofenac was not statistically significant. But this isn't the point of the graph. The chart clearly shows the superiority of DMSO as a penetrating agent versus water in aiding diclofenac to penetrate the skin barrier in this study.

General

Q. Now that we have new promotional material, will the territory table top display units be updated?

A. Yes. Our goal is to have the new table top graphic panels to the sales force by early/mid-May.

Q. Can we talk about other countries use of PENNSAID (similar to Jurnista and EXALGO)?

A. No. Since Covidien only owns the marketing and distribution rights to PENNSAID in the United States, we currently do not have access to data regarding its use in other countries.

Q. Has there been any thought to compare PENNSAID head-to-head with Voltaren Gel?

A. Due to a variety of reasons, there are no plans to conduct a head-to-head study against Voltaren Gel. However, we will continue to make a significant investment into the lifecycle of PENNSAID.

Q. Have there been any serious AE's reported to date?

A. There were some serious AEs reported during the clinical trials, but to date, no serious adverse events have been reported post-marketing with PENNSAID in the U.S.

Q. Can we get more stickers for the co-pay cards?

A. The \$60.00 PENNSAID co-pay stickers are now available at SmartSource, and can be ordered on-line. Please remember to order an equal amount of each type of sticker, as each card should receive one of each color. Order limits are set at 500 stickers per color.

Following are MK numbers for each:

MK30027 - Orange circle stickers (for front of card)

MK30028 - White rectangular stickers (for face of actual co-pay card)

Q. Can you provide us a status update on the new \$60 co-pay cards?

A. We are currently exploring different options on how best to position the new \$60 co-pay card. We will either have a revised, stand-alone piece or make the co-pay card part of a new patient starter kit. We will update the field once a final decision is made.

Q. Will there be any changes to the PENNSAID samples/carriers?

A. We are exploring several options of reformatting the current sample configuration. Once we have made a final decision we will update the field accordingly.

Q. Are we thinking about any other programs to help leverage the new co-pay card? (automatic discount at pharmacy, voucher, what are patients willing to pay?)

A. At this time, we believe we have adequately addressed what patients are willing to pay at the pharmacy with the new \$60 co-pay card. As a reminder, the objective of the card is to minimize patient out-of-pocket until our managed care tiering improves. Since the new card is only a few weeks old, it's still too early to determine if additional steps are needed for incremental discount programs. However, we are continuing to explore other viable options, and we implement if necessary.

Q. Does rubbing have anything to do with accelerating the penetration of topical agents?

A. As a reminder, do not attempt to answer any questions regarding Voltaren Gel. Please redirect your physician to their respective Endo sales representatives. When considering management of OA of the knee, part of the therapeutic process is for patients to rub or massage the painful area. Rubbing in topical agents, whether medicinal or not, will enhance penetration/absorption. However, it is unknown if any topical agent is more effective by rubbing.

Q. When will the patient tear off cards be available?

A. The new patient tear off sheets will incorporate the new patient dosing instructions and are currently in the process of being reviewed by PARC. The new pieces should be available to the field by end of April. In addition, shortly thereafter, we will also make these pieces available in Spanish.

Q. Can we sponsor any CME activities?

A. No, Covidien cannot sponsor CME programs as the sponsor is responsible for the content and delivery of CME programs and Covidien cannot do that both by its own policies and by the rules of the ACCME – the body that accredits CME programs. Covidien can, however, provide financial support to the sponsors of CME programs through its Educational Grant process. In that process, the evaluation and review of all CME grant requests is Medical Affairs responsibility as Sales and Marketing cannot be involved at all in the process. The rationale for these requirements are that CME programs must be independent and impartial so Covidien's role must be very narrow (evaluating and deciding on proposals created by sponsors) and removed as much as possible from promotional aspects of Sales and Marketing. Also, CME programs must be carefully distinguished from field-based promotional educational programs like Speaker Bureau activities which, in turn, need to also meet specific Covidien requirements.

REMS/CARES ALLIANCE

Q. Does EXALGO have a REMS?

A. Yes, there is an approved REMS with EXALGO that focuses on prescriber education. While training is not required as a prerequisite to prescribe EXALGO, Covidien believes open and effective communication is essential for health care professionals to safely and effectively prescribe EXALGO to appropriate opioid-tolerant patients.

Q: I heard you have a REMS with a patient registry/prescriber certification built in?

A: No, the EXALGO REMS has neither a patient registry nor a prescriber certification requirement; however, Covidien provides as part of the EXALGO REMS a medication guide for patients, voluntary prescriber education and essential risk & safe use information for EXALGO.

Q: When will I be able to order the EXALGO REMS materials on Smart Source?

A: You will be able to place these orders starting on May 3rd, 2010.

Q: What is in this EXALGO REMS?

A: Covidien is providing patients, when they come to the pharmacy, with a medication guide that discusses the safe and appropriate use of EXALGO. In addition, Covidien is providing a prescriber education program kit that discusses the safe and appropriate prescribing of EXALGO. Finally, Covidien is required to conduct periodic assessments on its efforts to determine whether prescribers and patients are receiving and understanding this important information about EXALGO.

Q: Is the prescriber education required?

A: Yes and no, so let me explain. While prescriber training is not a prerequisite to prescribe EXALGO, Covidien believes open and effective communication is essential for prescribers to safely and appropriately prescribe EXALGO to appropriate opioid-tolerant patients. We ask prescribers to spend some time reviewing the EXALGO prescriber brochure, which highlights this essential information about EXALGO. In turn, we ask that prescribers spend a few minutes completing the EXALGO Essential Information Form (EEIF) that reinforces this essential information about EXALGO.

Covidien strongly encourages prescribers to partner with us in order to reduce risks of abuse, misuse, overdose, and addiction that come with any long-acting opioid. We believe effective and open communication with healthcare professionals will do just that.

Q: Do I have to fill out this EXALGO Essential Information Form (EEIF)?

A: While prescriber training is not a prerequisite to prescribe EXALGO, Covidien believes open and effective communication is essential for health care professionals to safely and effectively prescribe EXALGO to appropriate opioid-tolerant patients. The FDA will review the number of completed EEIFs, and the percentage of correct answers from health care professionals as part of its assessment as to the effectiveness of Covidien's voluntary prescriber training (and thus the REMS). Completion of EEIFs provides Covidien with a view of this program's effectiveness, and will ideally allow us to continue to provide quality educational materials without additional burdens, such as prescriber certification and/or a patient registry.

Q: Can you just fill this EEIF form out for me?

A: No, I can't fill this form out for you. The EEIF is intended to ensure that you understand the key risks and safe use of EXALGO.

Q: Where can I get this EEIF form?

A: You can download, print, and fax or email the EEIF to 1-888-423-3511 or email to exalgocallcenter@unitedbioresource.com. Before you complete the EEIF, please review the EXALGO Prescriber Brochure, which you will find the essential information about EXALGO. You can download and print any EXALGO REMS material from our website www.exalgorems.com.

Q: I heard you can get free Scott Fishman book?

A: Yes, it is through our C*A*R*E*S Alliance Program, at no cost to you. C*A*R*E*S. Alliance is Covidien's outreach to prescribers, pharmacists, office staff, and patients to provide education and essential safety messages regarding all our prescription pain products. Would you also be interested in the American Pain Society and the American Academy of Pain Medicine – Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancerous Pain? If you would provide me your Name, Email, Practice, Address, City, State and Zip code, we will send these items to you.

Q: When did the REMS materials distribute to the physicians on our call-list?

A: The physician mailing (a.k.a M.D./alert) was completed on 4/21/2010. Your physicians should receive the material in 5 to 7 business days.

Q: When will I receive the initial EXALGO REMS package?

A: The auto shipment of the EXALGO REMS materials will begin the week of May 3rd, 2010.

Q: What will be in the EXALGO REMS package?

A: The package will contain (quantity):

Memo

EXALGO REMS Prescribing Education Program Kit (10)

EXALGO REMS Prescribing Brochure (10)

EXALGO Essential Information Forms (25)

EXALGO Medication guide tear pads (5 packs)

CARES Alliance Business Reply Card (BRC) (25)

Responsible Opioid Prescribing book by Scott Fishman (1)

Journal of Pain: Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain by APS (1)

Q: What can I order through Smart Source?

A: You can order all EXALGO REMS materials plus CARES Alliance BRC.

Q: Where can I find the EXALGO REMS and CARES Alliance materials on the Smart Source website?

A: Log onto Smart Source using this link <http://www.smartsourcellc.com/covidien/> and follow this path: Pharma Brand > EXALGO > REMS or CARES Alliance.

Q: Where can I find additional EXALGO MG Tear Pads on Smart Source?

A: Log onto the Smart Source site using this link <http://www.smartsourcellc.com/covidien/> and follow this path: Pharma Brand > EXALGO > REMS > EXR-008.

Q: Will I be notified when my target physicians complete their EEIF forms for the EXALGO REMS?

A: No, you will not be notified of whether an individual target has completed an EEIF. You will be given data about the number of EEIFs in your territory by zip code, but we do not want you to be pushing specific targets to complete an EEIF. Your role with regard to the EXALGO REMS is to provide the baseline education about it that is contained in your talking points and to make them aware of the EEIF. Once a target has told you that he/she has completed an EEIF, then you may accept that at face value and not discuss the issue again since you have completed your task. At that point for that target your responsibility with regard to REMs is only to answer questions.

SALES OPERATIONS

Q: What is the sample configuration for Pennsaid?

A: 1 unit = 6 bottles

Q: Can you sample less than 1 Pennsaid unit?

A: No, all samples must be recorded as a full unit and you cannot split up a unit.

Q: How many Pennsaid sample units can I leave a physician?

A: 3 units per physician visit.

Q: How often do I take inventory counts?

A: You will receive an email reminder from CovidienSA. Perform a physical count of your units at the end of your last day worked each month. Click on the hyperlink included in the email reminder to enter your physical inventory.

Q: What are the right sample forms to use for Pennsaid?

A: Pennsaid Direct Ship Request – MK8948; 1 page form used for sampling physicians who are not in your database.

Sample Request/Acknowledgement Form – MK8809; 3-part form used when your computer is unavailable to hand sample physicians who are in your database marked as “sample eligible.”

Sample Transaction Form – MK8813; 3-part form used for sample transfers, product returns and when your computer is down – Physical inventory counts and acknowledgement of delivery

Q: How do I correct E-Sig errors in Mobile Intelligence?

A: If a mistake is made on an e-signature document and the error is noticed on the same day:

1. Render a second e-signature document with the correct information and obtain a 2nd signature from the physician.
2. Send an email to Bev River or Liz Hudson. Include a brief explanation of the error including the physician's name and the date the error occurred. The incorrect e-signature document will be removed from Mobile Intelligence.

If you identify a mistake is made at a later date than when the e-signature document was rendered:

1. Complete a back-dated paper Sample Request/Acknowledgement Form (MK8809) and obtain the physician's signature.
2. Send an email to Bev River or Liz Hudson. Include a brief explanation of the error including the physician's name and the date the error occurred. The incorrect e-signature document will be removed from Mobile Intelligence.

Q: Should the sales force assist physicians in processing prior authorizations?

A: No. This is not an activity in which the sales force should engage.

SPEAKERS PROGRAMS

Q: Where do I find the Speaker program request and cancellation forms?

A: The link is as follows: \\tahaze-fs03\brandslibrary\KOL Consultant Program\Speaker Bureaus\Speaker Programs\Program Forms.

Q: What is the status of the doctor I referred?

A: The most up-to-date eligible speaker list can be found on the brands library in the Speaker Bureaus folder. If your doctor is not listed, his/her CV is still in the review process.

Q: Who do I contact about speaker issues not related to speaker programs? For example, slide decks, honoraria, etc.?

A: Donna (donna.richie-anderson@covidien.com) or Pennsaid@covidien.com or Exalgo@covidien.com.

Q: Where do I find Speaker Nomination forms and Program Cancellation forms?

A: On the Brands Library, open the following path: KOL Consultant Program >Speaker Bureaus->Speaker Programs->Program Forms.

Q: I have some updates to add to my program request (AV equipment, speaker equipment, new venue, change date, etc.). What do I do?

A: Call Selva at (518) 886-0819 for EXALGO and (518) 226-0818 for PENNSAID, but remember, fees may be incurred depending on the status of planning.

Q: The speaker I nominated is not on the eligible list so what should I do?

A: Select another speaker who is eligible to speak. If you submit the request with a speaker who is not eligible, your request will be sent back to you by your Covidien Speaker Bureau Coordinator for you to select another speaker. Once updated, your request will be forwarded to Selva for processing.

Q: When will the speaker I nominated be eligible?

A: That is largely dependent on the speaker. After we receive a signed contract from the speaker, we submit for in-house signatures, and then the speaker receives an email to register for a training session. About 24 - 48 hours after training, the speaker will become available.

Q: Can I schedule a program if the speaker will be trained by the date of the program?

A: You can submit a program any time. However, AHM will not be able to do the necessary work to set-up the program until a trained speaker is confirmed. So you may not have access to any invitations for the program depending on when the speaker successfully completes training. This may not be optimal for a successful program.

Q: When will I receive invitations for my program?

A: Invitations cannot be generated until both **speaker and venue** are confirmed.

If you turn your request in 6-8 weeks prior to the program, you should have your invitations about 4 weeks prior to the program. For requests submitted 4 weeks prior to the program, the invitations should be ready about 2 1/2 - 3 weeks prior to the program, depending on speaker/venue response time.

Pharmacy Related Questions:

EXALGO

Q: How often are scheduled narcotics ordered at a pharmacy?

A: Generally this is weekly, however depending on the pharmacy, they may have one specific person who orders who may not always be in the store, or they may choose to order only on one specific day or days for better security for these controlled substances. We have heard that some pharmacies like to wait to order until they have enough products needed to fill up an entire 222 form (10 line items). Since this can vary you should ask the pharmacy their rules and also ask if there are exceptions.

Q: Can a pharmacy order scheduled products whenever they have a need?

A: Yes – we have talked to all of our major wholesalers and they have no limitation on when pharmacies can order scheduled products or when they can ship them. Generally, deliveries do not occur on the weekend, but even this can sometimes happen. The only limitation may be store level policies or rules that they like to adhere to, but these are not due to the wholesaler, the required 222 form can be processed daily if needed (individual pharmacy decision).

Q: How long does it take for a pharmacy to receive their scheduled products from their wholesaler?

A: Depends on the pharmacy – general rule is 3 to 5 business days. This is because the hard copy 222 needs to be received at the wholesaler before they can ship the product, sometimes a weekend may fall during the delivery and delay it even more. Often this form is sent overnight, which speeds the process. In the future an electronic system CSOS (controlled substances ordering system) will be widely available and will eliminate these hard copy forms and mailing. Ask your pharmacies what is their average lead time for ordering controlled substances (CII).

PENNSAID

Q: If a non-scheduled product, like PENNSAID, is not in inventory at the pharmacy, when can it be ordered?

A: Non-scheduled products can be ordered anytime via a pharmacies' computer – no paper form or special person is required. For example: Once a script gets adjudicated at the point of sale; it can be ordered automatically from their wholesaler. Depending on that stores delivery schedule, it is usually next day delivery. Some of our pharmacy chains that are warehousing PENNSAID will have what is called auto-replenishment where new product is automatically ordered as soon as store inventory hits a certain point. Again, engage your pharmacy customers with these type questions to learn more about their store. Tell them that you will relay this information to your targeted physicians.